Claims 1-22, 27-30 and 39 stand rejected under 35 USC 103(a) as being unpatentable over Loosmore et al in view of Menozzi et al. The rejection is traversed.

As explained in the previous response, the recombinant DNA of claim 1 comprises a sequence (1) coding for a polypeptide heterologous with respect to Fha, fused in the same reading frame with a sequence (2) coding for at least a part of the precursor of the Fha. The polypeptide encoded by a recombinant DNA of Claim 1 therefore qualifies as a "fusion protein", i.e., "a protein containing amino acid sequences from each of two distinct proteins" (see the attached abstract from the "Dictionary of Microbiology and Molecular Biology", published in 1987 by John Wiley & Sons).

The Examiner's attention is respectfully drawn to the fact that although a fusion protein is always encoded by a fusion gene (i.e., a gene comprising nucleotide sequences from two distinct genes), a fusion gene does not necessarily encode a fusion protein. In particular, when the fusion gene consists in a promoter from a fist gene (promoter A), driving the transcription of a coding sequence from a second gene (coding sequence B), the protein encoded by the fusion gene is not a fusion protein.

The fusion genes disclosed by Loosmore et al consist in "a structural pertussis gene fused at an ATG start codon to a native but autologous pertussis promoter". Examples of such fusion genes are given in column 2, lines 18 to 23. None of the fusion genes disclosed in this document encode fusion proteins according to the above definition.

The Examiner notes that the polypeptide expressed by Loosmore's recombinant gene can be a "polypeptide heterologous with respect to Fha", for example, when the involved structural gene is the PRN structural gene. However, a fusion gene according to Loosmore et al and comprising the PRN structural gene, even in combination with the Fha promoter, does not encode a fusion protein, since the encoded polypeptide does not comprise an amino acid sequence from a protein distinct from PRN.

Therefore, Applicants respectfully submit that there is nothing in Loosmore et al that describes or suggests the construction of a recombinant DNA encoding a fusion protein comprising an amino acid sequence from Fha fused to an amino acid sequence from a protein distinct from Fha. There is also nothing in Loosmore et al that would have provided the skilled artisan with any motivation to make fusion proteins as those encoded by the recombinant DNA of claim 1, since Loosmore et al only deals with the

optimization of native antigen production in *B. pertussis* strains for the vaccination against *B. pertussis*.

With regard to the reference of Menozzi et al, Applicants respectfully submit that it does not remedy the deficiencies of the primary reference. Indeed, as explained in the last response, Menozzi et al report a fundamental study of the Fha-heparin interactions. They also teach a method to purify Fha using heparin as ligand in an affinity chromatography procedure. The Examiner ntoes that the hybrid gene of Loosmore et al can express Fha that contains the heparin interaction site. However, Applicants respectfully submit that a Fha expressed by a gene as described in Loosmore et al does indeed contain the heparin site, but does not comprise an amino acid sequence from a protein heterologous to said Fha. Therefore, a hybrid gene as described in Loosmore et al, even in view of Menozzi et al, does not suggest the present invention.

Moreover, there is nothing in Menozzi et al that could have led the skilled artisan to construct fusion proteins comprising a Fha moiety and a moiety heterologous to Fha, much less to reasonably expect that such fusion proteins would exhibit advantageous immunogenic properties as those of the present invention.

From the above, Applicants respectfully submit that Loosmore et al and Menozzi et al, either alone or in combination, would not have provided the skilled artisan with any motivation to construct chimeric proteins comprising a Fha moiety.

The subject matter of claims 1-22, 27-31 and 39 would therefore not have been obvious having regard to Loosmore et al and Menozzi et al. Withdrawal of the rejection is hence respectfully requested.

Claims 34, 35 and 37 stand rejected under 35 USC 103(a) as being unpatentable over Loosmore et al in view of Menozzi et al and Locht et al. The rejection is traversed.

Claim 34 pertains to a recombinant DNA encoding a fusion protein comprising a Fha moiety fused to a polypeptide heterologous with respect to Fha, the resulting fusion protein being able to facilitate the presentation of the antigen comprised in the heterologous polyppetide to the mucosal immune system.

Claim 35 pertains to a vaccine composition comprising cells, the cells comprising a recombinant DNA encoding a fusion protein containing a Fha moiety and a moiety heterologous with respect to Fha.

The Examiner states that the immunogenic characteristics of Fha taught by Locht et al would have led

the skilled artisan to present Loosmore's composition as modified by Menozzi et al to the mucosal immune system to produce the instant invention.

However, as explained above, Loosmore's composition does not comprise a fusion protein, even though it comprises a protein expressed by a fusion gene (promoter A/coding sequence sequence B). There is nothing in Loosmore et al, nor in Menozzi et al, that suggests making compositions containing fusion proteins with a Fha moiety. The teaching of Locht et al does not remedy the deficiencies of the previous references, since there is nothing in Locht et al that suggests making fusion proteins as in the present invention.

Therefore, it is respectfully submitted that Loosmore et al, Menozzi et al and Locht et al, either alone or in combination, would not have led the skilled artisan to the invention claimed in claims 34, 35 and 37. Withdrawal of the rejection is hence respectfully requested.

Claim 39 stands rejected under 35 USC 103(a) as being unpatentable over Loosmore et al in view of Menozzi et al. Withdrawal of this rejection is respectfully requested for the reasons set forth in the above.

This application is submitted to be in condition for allowance and a Notice to that effect is requested.

Respectfully submitted,

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